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EXAMINER

WOITACH, JOSEPH T

ART UNIT PAPER NUMBER

1632

DATE MAILED: 04/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/855,587

Applicant(s)

SASAI ET AL

Examiner

Joseph T. Voitach

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 03 December 2004.  
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,2,12-15,18-24,26,27,56,57,72 and 73 is/are pending in the application.  
4a) Of the above claim(s) 22,56 and 57 is/are withdrawn from consideration.  
5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
6) ☒ Claim(s) 1,2,12-15,18-24,26,27,56,57,72 and 73 is/are rejected.  
7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.  
10) ☒ The drawing(s) filed on 16 May 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☒ All b) ☐ Some \* c) ☐ None of:  
1. ☒ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_.  
5) ☐ Notice of Informal Patent Application (PTO-152)  
6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

This application claims benefit to provisional application 60/257,049, filed December 20, 2000, and to foreign applications: 1000-144059, filed May 16, 2000; and 2000-290819, filed September 25, 2000, both filed in Japan.

Applicants amendment filed December 3, 2004, has been received and entered. Claims 1, 12-15, 18-21, 23, 24, 26, 27, 56, 57, 72 have been amended. Claim 73 has been added. Claims 3-11, 16, 17, 25, 28-55 and 58-71 have been cancelled. Claims 1, 2, 12-15, 18-24, 26-27, 56, 57 and 72 are pending.

### ***Election/Restrictions***

Claims 1, 2, 12-15, 18-24, 26, 27, 56, 57, 72 and 73 are pending. Newly added claim 73 encompasses the use of specific cell lines in the elected invention, therefore will be examined with the elected invention. Claims 21, 56 and 57 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 13. See office action mailed January 16, 2003.

It is noted that the election of species was required, in particular the species of (C) ectodermal cell (and generally with respect to the other species to cells of the nervous system) and the species of (Q) BMP4 was elected (see election page 2). Claims 1, 2, 12-15, 18-20, 22-24, 26-27 and 72 are currently under examination.

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Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 72 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn.

The amendment to the claims to indicate that the cell used is a stroma cell not a stem cell, and applicants arguments that the recited cells are readily available has addressed the basis of the rejection. Specifically, it was set forth that stem cells with the names recited in the claim did not appear to exist except for the disclosure, therefore were required to be deposited. In light of the amendment to the claim, Examiner agrees that the cells recited in the claim represent widely available cell lines known in the art.

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Claims 12-15, 18-20, 23, 24, 26-27, 72 and 73 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". Specifically, the claims have been amended to recite and encompass a specific combination of non-aggregation conditions under specific culturing conditions where retinoic acid is absent and BMP is either present (claim 12) or absent (claim 13) and requiring the additions of a stromal cell-derived factor. Applicants point to several portions and the working examples in the specification for support of the amendment. Review of all the citations does not indicate provide literal support for the absence of retinoic acid. Further, while page 41, lines 22-25 indicate to add BMP4 for epidermal differentiation, lines 26-35 indicate the removal of BMP4, there is no specific recitation for the specific combination of all the elements now recited in the claims. Moreover, there is no description of any specific stroma-derived factor that would or should be added, or any methods to obtain such a factor from a cell.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 12-15, 18-20, 23, 24, 26-27, 72 and 73 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described. As noted above, the specification fails to specifically provide what stroma cell-derived factor is added in the claimed methods, or what the

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factor does and methods to obtain such a factor. While the specification broadly supports growing cells on stroma cells, it fails to provide the necessary guidance to produce the unknown factor provided by these cells for use in the methods as claimed.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

Claims 1, 2, 12-15, 18-21, 23, 24, 26-27 and 72 stand rejected and newly added claims 73 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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Applicants note that the affect of BMP4 depends on the type of stroal cell used and the timing and addition of BMP4 to the culture. Applicants argue that the issues raised in the basis of the rejection have been addressed in the amendment to the claims. See Applicants amendment, middle page 8. Applicants arguments have been fully considered, but not found persuasive.

The embodiments under examination as represented by the election of species of differentiation into(C) ectodermal cells, in particular neural cells, and the use of the specific factor of (Q) BMP4 was elected. The basis of the rejection focuses on these two species and the evidence in the art that BMP4 acts as an antineuralizing morphogen. The claims are broad and encompass simply culturing on any stroma cell, or any stroma cell derived factor without providing any guidance to specific stroma cells or the specific factors that are required. As noted previously, even in the post-filing art the factor that some stroma cells may provide to affect differentiation is not presently known. Mizuseki *et al.* (PNAS, 2003) provide a similar teaching for the affect of BMP4 in the culture, however provides evidence that the affect of BMP4 is complex and dependent on the stromal cell used and the time that BMP4 is added to the co-culture. At the time of filing Kawasaki *et al.* (Neuron 2000) teach that different stromal cells and cell lines can provide undefined factors termed SDIAs that allow for the differentiation of mouse ES cells (see summary in abstract). Review of the teaching of the instant disclosure provides similar guidance and examples as that provided by Kawasaki *et al.* While the post filing art by both Kawasaki *et al.* and Mizuseki *et al.* teach that BMP4 when added to ES cells promotes epidermogenesis (Mizuseki *et al.*, page 5832, second column, Discussion section), not the formation of ectoderm cells or a more differentiated neural cell type. Case law teaches (*Ex parte*

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*Forman*, 230 USPQ 546,547 (BPAI 1986)) that “the disclosure of a patent application must enable practice of the invention claimed without undue experimentation”, wherein factors involved in the determination of undue experimentation were deemed to include “the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims.” Further, the specification must teach those of skill in the art how to make and how to use the invention as broadly claimed. *In re Goodman*, 29 USPQ2d at 2013 (Fed. Cir. 1994), citing *In re Vaeck*, 20 USPQ2d at 1445 (Fed. Cir. 1991). In the instant case, the specification fails to provide the necessary guidance to practice the claimed invention as broadly claimed. The amendment to the claims is noted, however the amendments fail to address the issue of using any stroma cell known in the art, in particular because the factors they provide are not disclosed in the specification and still are not known in the art as evidenced by the art of record.

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to make and/or use the invention as claimed.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.



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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 14, 18-21, 23, 24, 26, 27 rejected under 35 U.S.C. 102(b) as being anticipated by Thomson (US patent 5,843,780) is withdrawn.

It is noted that the claims have been amended to recite *in vitro*, as such the in vivo methods of forming a teratoma taught by Thomson do not anticipate these amended claims. The *in vitro* conditions taught by Thomson fail to set forth the specific conditions now recited in the amended claims.

Claims 1, 2, 14, 18-21, 23, 24, 26, 27 rejected under 35 U.S.C. 102(a/e) as being anticipated by Samarut *et al.* (US patent 6,114,168) is withdrawn.

As discussed above, the amendment to the claims to encompass cultures in vitro have distinguished the methods from those of Samarut *et al.* who teach the use of in vivo injection to produce teratomas with various differentiated cell types. Moreover, the specific conditions for the presence or absence of various factors for the production of a specific cell type are not present even inherently in the methods of Samarut *et al.*

Claims 1, 2, 12-15, 18-24, 26-27, 56, 57 and 72 rejected under 35 U.S.C. 102(a) as being anticipated by Kawasaki *et al.* (Neuron, 2000) is withdrawn.

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In review of the translation of the foreign priority documents Examiner agrees that they provide adequate support for the claimed invention. See also Applicants' amendment, page 8. Since Kawasaki *et al.* reference date is after the filing date of the foreign applications, it no longer qualifies as a 102(a) type reference.

### ***Conclusion***

No claim is allowed. The claims are free of the art of record because the art fails to teach the specific *in vitro* conditions that result in epidermal differentiation required by the claims, however they are subject to other rejections.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

*Joseph T. Woitach*  
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